NTP
National Toxicology Program

Polycyclic Aromatic Hydrocarbons Research Concept: Introduction

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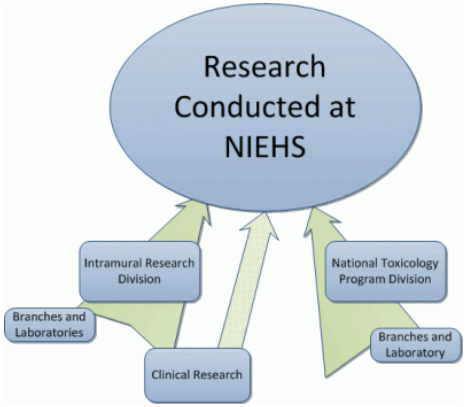
NTP Board of Scientific Counselors Meeting
December 11, 2012

Development of NTP Research Programs

- In response to external nominations or initiated by NIEHS/NTP
  - Review the science and identify knowledge gaps
  - Consultation with agency partners, scientific experts
  - Multiple levels of review to determine merit and priority for study
  - Not all nominations lead to a research program



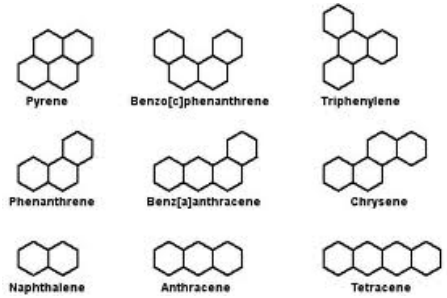
- Iterative approach to study design, conduct and analysis
  - Phased programs with multiple review and decision points
- Incorporate novel and alternative testing approaches
  - Inform and prioritize chemical and study endpoint selection
  - Integration and interpretation of multiple data types

NTP Research Concepts

- A brief document outlining:
  - Rationale, data gaps, key issues, specific aims to address
  - Proposed approach to address toxicological data needs for specific substance or issue
    - Not experimental study design
  - Significance and and expected outcome of a proposed research program
- Facilitate internal and external review of projects in the NTP research and testing program
  - Sufficient detail to understand scope, strategy and direction

Origin of PAH Research Program

- A very large class: many agents, many exposure sources and pathways, many effects of concern, many gaps
- Very little NTP testing to date
  - NCTR, NIOSH
- Prior nominations
  - Benzo(a)pyrene (CalEPA)
    - Need for reliable quantitative risk assessment data
  - PAHs oral studies (Health & Welfare Canada)
    - Lack of quantitative carcinogenicity data by the oral route; little attention has been paid to reproductive and immunotoxic effects
  - PAH quinones (Academic researcher)
    - Released into the environment from incomplete combustion of organic materials including wood and fossil fuels; high potency for generating reactive oxygen species; possible role in inflammatory diseases



Origin of PAH Research Program (2)

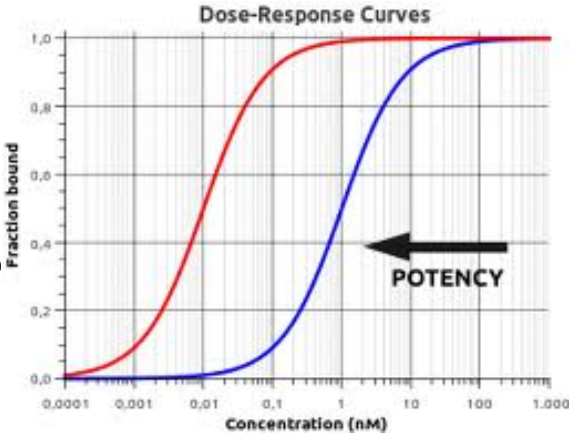
- Issues driving current project
  - Need to expand database for relative potency factor development and cumulative risk assessment
  - Research/data needs expressed by other organizations
  - Gulf Oil Spill concerns and lack of data on PAH subclasses
  - New (and old) sources of exposure

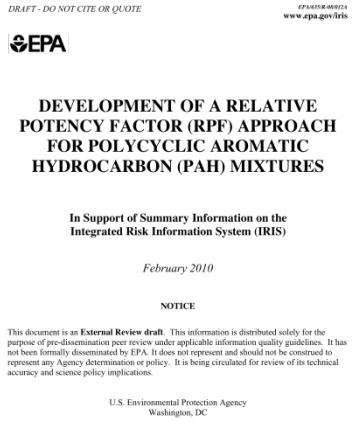
Development of PAH Relative Potency Factors

- EPA Peer Consultation Workshop on Approaches to Polycyclic Aromatic Hydrocarbon (PAH) Health Assessment (2002)

  …the following testing should be prioritized: (1) …whether…other PAHs that might be more toxic/more prevalent in PAH mixtures, and thus more appropriate for testing and use as a reference; (2) what chemicals should be presented to NTP for testing; (3) whether recommendations for testing should be for individual PAHs or for complex mixtures (e.g., diesel fuel, coke oven emissions, and others). In addition, the list of relevant PAHs should be revisited — better data and a longer list of compounds are needed.

- EPA IRIS Relative Potency Factor Approach for PAH Mixtures (External Review Draft Feb 2010)
  - Developed draft RPFs for 27 PAHs
  - Science Advisory Board review (March 2011) recommended NTP testing of a portfolio of complex PAH mixtures





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EPA/635/R-06/012A
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EPA

DEVELOPMENT OF A RELATIVE POTENCY FACTOR (RPF) APPROACH FOR POLYCYCLIC AROMATIC HYDROCARBON (PAH) MIXTURES

In Support of Summary Information on the Integrated Risk Information System (IRIS)

February 2010

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U.S. Environmental Protection Agency
Washington, DC

PAHs in Crude Oil

- Carcinogenic combustion-related PAHs at low levels
- Alkyl PAHs typically 5-10 fold > parent
  - Relative concentration increases with weathering
- NTP analytical chemistry analyses of Deepwater Horizon source oil and oiled environmental samples from Gulf region

	MC252 Source Oil [Average Q4000] (mg/kg)	Gulf seafood highest value ppm [FDA web]	Average carcinogenicity RPF, EPA Feb 2010 (draft)	IARC 2010 overall
Acenaphthene	14.9		-	3
Acenaphthylene	8.6		-	-
Anthracene	11.7	0.001410	0	3
Benz(a)anthracene	7.0	0.002803	0.2	2B
Benzo(a)pyrene	2.3	0.010090	1	1
Benzo(b)fluoranthene	6.5	0.002080	0.8	2B
Benzo[e]pyrene	12.5		-	3
Benzo(g,h,i)perylene	2.1		0.009	3
Benzo(k)fluoranthene*	0.0	0.001650	0.03	2B
Dibenz(a,h)anthracene*	2.2	0.000560	10	2A
Indeno(1,2,3-cd)pyrene	0.0	0.001740	0.07	2B
Perylene	0.1		-	3
Chrysene	54.5	0.003660	0.1	2B
C1-Chrysenes	119.2		-	-
C2-Chrysenes	139.7		-	-
C3-Chrysenes	103.1		-	-
C4-Chrysenes	68.8		-	-
Dibenzothiophene	59.8		-	-
C1-Dibenzothiophene	180.9		-	-
C2-Dibenzothiophene	257.6		-	-
C3-Dibenzothiophene	181.7		-	-
C4-Dibenzothiophene	82.0		-	-
Fluoranthene	4.4	0.767650	0.08	3
C1-fluoranthenes	91.1		-	-
C2-fluoranthenes	146.9		-	-
C3-fluoranthenes	165.1		-	-
Fluorene	159.4	0.620000	-	3
C1-Fluorenes	361.0		-	-
C2-Fluorenes	475.0		-	-
C3-Fluorenes	370.1		-	-
Naphthalene	848.3	0.152000	-	2B (2002)
C1-Naphthalenes	1951.3		-	-
C2-Naphthalenes	2500.3		-	-
C3-Naphthalenes	1690.0		-	-
C4-Naphthalenes	859.7		-	-
Phenanthrene	327.5	5.240000	0	3
C1-Phenanthrenes	750.1		-	-
C2-Phenanthrenes	826.5		-	-
C3-Phenanthrenes	495.6		-	-
C4-Phenanthrenes	195.0		-	-
Pyrene	17.6	0.004260	0	3
C1-Pyrenes	*91.1*		-	-
C2-Pyrenes	*146.9*		-	-
C3-Pyrenes	*165.1*		-	-

Gulf Oil Spill: PAHs as Toxic Crude Oil Chemical Indicators

- Safety of Gulf seafood based on levels of concern for:
  - 7 carcinogenic PAHs: Benzo(a)pyrene, benz(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, chrysene, dibenz(a,h)anthracene, indeno(1,2,3-c,d)pyrene
  - 5 non-carcinogenic PAHs: Naphthalene, pyrene, fluorene, fluoranthene, anthracene/phenanthrene
- Federal Interagency Toxicology Workshop
  - Significant knowledge gaps identified: more data needed to inform risk assessment of petroleum PAHs

PNAS

SPECIAL FEATURE

ENVIRONMENTAL SCIENCES

Federal seafood safety response to the *Deepwater Horizon* oil spill

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Edited by Marcia K. McNutt, US Geological Survey, Reston, VA, and approved January 11, 2012 (received for review June 2, 2011)

Following the 2010 *Deepwater Horizon* oil spill, petroleum-related compounds and chemical dispersants were detected in the waters of the Gulf of Mexico. As a result, there was concern about the risk to human health through consumption of contaminated seafood in the region. Federal and Gulf Coast State agencies worked together on a sampling plan and analytical protocols to determine whether seafood was safe to eat and acceptable for sale in the marketplace. Sensory and chemical methods were used to measure polycyclic aromatic hydrocarbons (PAHs) and dispersant in >8,000 seafood specimens collected in federal waters of the Gulf. Overall, individual PAHs and the dispersant component dioctyl sodium sulfosuccinate were found in low concentrations or below the limits of quantitation. When detected, the concentrations were at least two orders of magnitude lower than the level of concern for human health risk. Once an area closed to fishing was free of visibly floating oil and all sensory and chemical results for the seafood species within an area met the criteria for reopening, that area was eligible to be reopened. On April 19, 2011 the area around the wellhead was the last area in federal waters to be reopened nearly 1 y after the spill began. However, as of November 9, 2011, some state waters off the Louisiana coast (Barataria Bay and the Delta region) remain closed to fishing.

On April 22, 2010, 2 d after the explosion on the *Deepwater Horizon* (DWH) drilling platform, the rig collapsed and the wellhead failed. The explosion resulted in the loss of human life and the uncontrolled release of >200 million gallons of Louisiana light crude oil occurring ~5,000 feet below the sea surface. DWH was declared a *Spill of National Significance* on April 29, 2010 and became the largest oil spill in US history (1). Among the significant human and environmental impacts of the spill, marine fisheries and supporting marine and estuarine ecosystems were subjected to contamination by crude oil, compromising the safety of seafood resources (1). An immediate and coordinated federal and state response ensued to safeguard seafood safety. Federal and state agencies mobilized personnel and resources to begin sampling seafood on April 28, 2010. Federal and state fishery closures were guided by observations of where oil was seen and forecasted to spread on the basis of climatic and hydrographic models (2). Seafood was collected around the periphery of the closed areas and from dockside and seafood market outlets across the Gulf coast and analyzed for oil-spill related contaminants to assess the effectiveness of the fishery closures. When the flow of oil was stopped on July 15, 2010 and the oil began to dissipate, sampling and analyses were conducted to determine whether seafood from previously closed areas was safe for harvest and human consumption. Sampling of reopened areas in federal waters continued through June 2011. We describe how federal agencies, working with the states, developed seafood safety criteria and protocols. In addition, sampling schemes, analyses, and data reporting for seafood safety efforts conducted in federal waters are provided. Results of testing the seafood collected in federal waters are also discussed.

Collaboration Among Federal and State Agencies to Develop a Protocol

The US Food and Drug Administration (FDA) operates a mandatory hazard analysis and critical control point (HACCP) safety program for all fish and fishery products under the provisions of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 *et seq.*), the Public Health Service Act (42 U.S.C. 201 *et seq.*), and related regulations. The National Oceanic and Atmospheric Administration (NOAA), under provisions of the Magnuson–Stevens Fishery Conservation and Management Act (16 U.S.C. 1801 *et seq.*), has the authority to close and open, with concurrence of the FDA, federal waters for seafood harvest. Marine resource and public health agencies of states bordering the Gulf of Mexico retain jurisdiction and responsibility for the health and safety of fish and fishery products within their respective territorial waters (3 miles from coastline except for Florida, which is 9 miles from coastline). Under these guidelines, should an oil spill occur, federal and state agencies, including the NOAA and the FDA, determine whether seafood is at risk for contamination and, if so, when seafood from a previously contaminated area may once again be safe for harvest and human consumption.

As the oil spread and fisheries were closed as a result of the spill, scientists and risk managers from all of the affected state and federal agencies convened to develop a comprehensive protocol to ensure the safety of Gulf seafood before impacted areas could be reopened for harvest for the American public. The NOAA publication titled *Managing Seafood Safety After an Oil Spill* provides agencies guidance in such situations (3). This guidance and current information from the FDA, the NOAA, the Environmental Protection Agency (EPA), the Centers for Disease Control and Prevention, and counterpart Gulf state agencies were used to establish a unified DWH seafood protocol (4). The DWH seafood safety risk assessment, an integral component of the protocol, was built upon an approach taken by the FDA in 1990 after the *Exxon Valdez* oil spill in Prince William Sound, Alaska (3). The protocol was implemented, by agreement of all federal and state authorities, in the reopening of commercial and recreational fisheries in both federal and state waters.

Author contributions: G.M.Y., M.M.K., W.W.D., J.E.S., C.C.W., E.S.G., L.L.D., K.M.M., B.T.N., S.W., N.B.B., R.A.B., P.N.K., and R.W.D. designed research; C.L.L. performed research; and G.M.Y., M.M.K., W.W.D., J.E.S., S.W., N.B.B., and R.W.D. wrote the paper.

The authors declare no conflict of interest.

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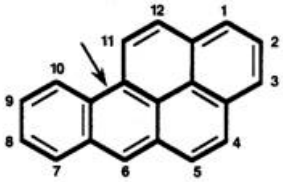
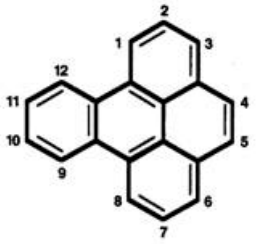
This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1108886109/-/DCSupplemental.

International Assessments

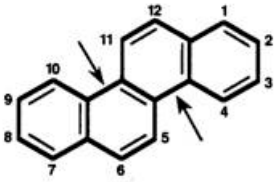
- IARC (2010) evaluated 60 PAHs
  - 45 classified as Group 3
- European Food Safety Authority (2008) Scientific Panel recommendations:
  - Toxicological data for individual PAHs as well as oral carcinogenicity data with mixtures relevant for dietary exposure are needed
  - Additional carcinogenicity and occurrence data for benzo[c]fluorene are needed



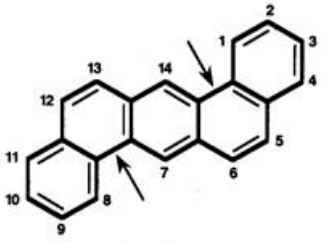
Benzo[*a*]pyrene



Benzo[*e*]pyrene



Chrysene

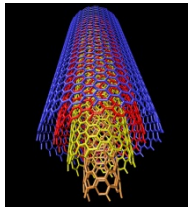


Dibenz[*a,h*]anthracene

Scientific Opinion of the Panel on Contaminants in the Food Chain on a request from the European Commission on Polycyclic Aromatic Hydrocarbons in Food. The EFSA Journal (2008) 724, 1-114.

A Recurring Source of Environmental Concern

- Coal tar sealants
- Energy extraction
  - Coal bed methane, mountain top removal mining, oil sands
- Carbon nanofiber / nanotube manufacturing
  - Birch *Ann Occ Hyg* 2011
- Synthetic turf playing fields



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Exposure and Emissions Monitoring during Carbon Nanofiber Production—Part II: Polycyclic Aromatic Hydrocarbons

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Production of carbon nanofibers and nanotubes (CNFs/CNTs) and their composite products is increasing globally. High-volume production may increase the exposure risks for workers who

USGS
science for a changing world

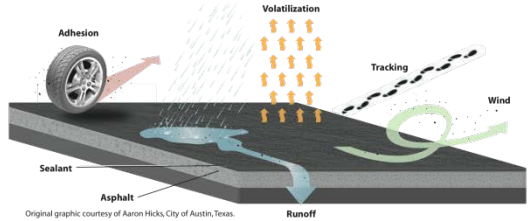
Coal-Tar-Based Pavement Sealcoat, Polycyclic Aromatic Hydrocarbons (PAHs), and Environmental Health

Studies by the U.S. Geological Survey (USGS) have identified coal-tar-based sealcoat—the black, viscous liquid sprayed or painted on asphalt pavement such as parking lots—as a major source of polycyclic aromatic hydrocarbon (PAH) contamination in urban areas for large parts of the Nation. Several PAHs are suspected human carcinogens and are toxic to aquatic life.

Sealcoat is the black, viscous liquid sprayed or painted on the asphalt pavement of many parking lots, driveways, and playgrounds.

Key Findings

- Dust from pavement with coal-tar-based sealcoat has greatly elevated PAH concentrations compared to dust from unsealed pavement.
- Coal-tar-based sealcoat is the largest source of PAH contamination to 40 urban lakes studied, accounting for one-half of all PAH inputs.
- Coal-tar-based sealcoat use is the primary cause of upward trends in PAHs, since the 1960s, in urban lake sediment.
- Residences adjacent to parking lots with coal-tar-based sealcoat have PAH concentrations in house dust that are 25 times higher than those in house dust in residences adjacent to parking lots without coal-tar-based sealcoat.
- PAHs move from a sealcoated surface into our environment by many mechanisms: storm runoff, adhesion to tires, wind, foot traffic, and volatilization.



Original graphic courtesy of Aaron Hicks, City of Austin, Texas.

U.S. Department of the Interior
U.S. Geological Survey

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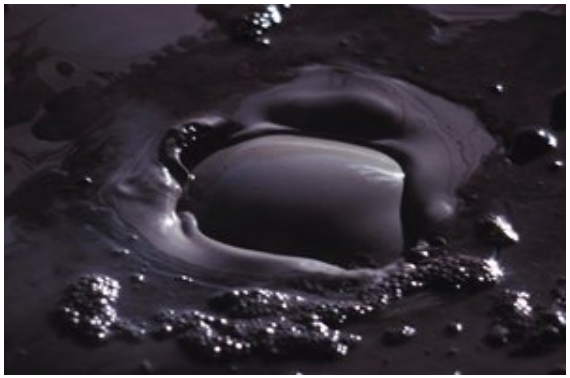
Fact Sheet 2011–3010
February 2011

Evolution of PAH Research Program

- This program is different
  - Model for future complex research programs
  - Use best tools available to address larger problems
- Development of research concept
  - Internal scoping
  - Consultation with agency partners early, going forward
- Choices made on scope and strategy to
  - Assemble a workable testing framework
  - Maintain flexibility for periodic adjustments
  - Add value to heavily researched area
  - Leverage other ongoing efforts



Todays Session

- Review and comment on draft research concept and determine whether the proposed research project is an appropriate use of NTP testing program resources
- Public comments
- Segmented presentation by project leader Dr. Cynthia Rider
  - Pause for clarifying questions, response to charge questions
- Comments from assigned Board reviewers
- Board discussion

Questions and Comments